

FIG. 1

```

1  agttgagtcgcaatagtggtggcgaacttca aatgcccttactgtccggaacaaccacca ttgccagggtgtgcaggccagatttgtta
91  atttgtgaaaagtggaaaaatttattccg ctaatgcctaacggaagagcccgcaagaaga ggccggacagaagactttccagctcttcgg
181 catctgaaaacgatagtgactccgagagcg tgaccagtgtagcaggaagagcagccggatg cgcccgaaacatacacaatagatggcctgg
271 acacgcaagaggtgtctgacagcacacagg tgagactccaacagctgaacgcagacaggt ttggccagcatagagcaaacgctttcaggca
361 acctcaactggacataaacgcagtagcgc agatagatgatgtgcgtgagcagctgcaga acgagtatttgaagaaatgtctgtcacat
451 attctgaggacctggatgctgctgcgtcaga aaaccgatttcaaggaaaactcactcaaaa ccctcgcccgctctctcaagagagcgga
541 acatatitgatgatggaactctcaagtcgc tagttgagtgatgtatatgataatgtctaa ttttaatttcatcagtggtgcaagatctgg
631 gcttagccgttctaaatggtatattcaggg ttgtcaagccacattttaaattaccoccatc ggtttttaaattctattgttagaaattagg
721 atctacatagaggtagagtgagcaacagaa cattgtttgctatccgggcccctccgactgg aacgtcttaccttcagctactatttattca
811 gaaaaaagagtgcattttcatctatcaagg tctcaagtgctgaatcaaatcactagtat tttttccgagactaaaaaaagttagacaca

901  ATGAAAGTTGCTACACTGTTTTCTTGGCT TCGAGTGTCTGTGTGCTGGGAGACCCACAG TTCGTGAAACTGGAGGCTCTGTTCTTCGG
① M K V A T L F F L A S S V C V I G D P Q F V K L E A S V L R
991  GGATCCACTTACAAGGATCCGAGAAGGGG GCCAAGCCGTTTCATGTTGGAAAAGAGGGCT GATGACGGCTCGGTACGATGGAATTCGAG
G S T Y K D S Q K G A K P F M L E K R A D D G S V T M E L Q
1081 AACGCCAGTCTTTCTACCAAGTCGAGATC GAGATAGGATCTGATAAGCAGAAGGTGGGG GTTTTGATTGATACCGGTTCTCGGACTTG
N A Q S F Y Q V E I E I G S D K Q K V G V L I D T G S S D L
1171 TGGGTGATGAACTCGAATAACTCTTACTGT TCGTCTCCAGCACTAAAAAATTGAAACGG GACGGACCGGCGATGCGCTACAAAAAGGA
W V M N S N N S Y C S S S T A Q K L K R D G P A D A L Q K G
1260 CGCGATCTTTCCGACCTGTACAATTTCAAC TCTCCAACGAAGACAACAAATGCAAAAGGA TTCTTGGGTGGCTGGGAGACTTGACCACA
R D L S D L Y N F N S P N E D N N A K G F L G G W G D L T T
1351 GTAGAGACTGCAACCCAGGATGAGACACAG ACGGCTCTCGTGCAGGCCACCGTGGAC TGCTCGCTATACGGAACGTTCAATCCTTCA
V E T A T Q D E T Q T A L A Q A T V D C S L Y G T F L Q K Y
1441 ACGTCCAATTCGTTCCACAACAACGGCAACC ACATTTGAGATTTCTGACGGGACCGCACT TTTGCCCGTGGAACTGGGGCTACGATGAT
T S N S F H N N G T T F E I S Y A D R T F A R G T W G Y D D
1531 GTCACCTTTCAATGGTGTACGGTTAACGAT CTCTCGTTGGCCGTGGCAGATGAAACAGAT TCTTCGACTGGTGTGTTTGGTATCGGATTG
V T F N G V T V N D L S L A V A D E T D S S T G V F G L
1621 AGGGAATTGGAACACACATACTCAGGAGGC GGACCAAGCATTACATCTACGACAACCTTA CCTTTCAAAATGGTCGACCGGAGTATC
R E L E T T Y S G G G P Q H Y I Y D N L P F K M V D Q G L I
1711 AATAGAGCGCCTATTCCGCTACCTGAAC TCAACTGAGTCCAGCACTGCCTCGATCCTC TTCGGTGCGGTTGACCAAGCAAATATACC
N R A A Y S V Y L N S T E S T A S I L F G A V D Q S K Y T
1801 GGAAGTCTTGGCTTCTCTCATCAAC ACGGCTGCTTCTACGGTTACCAAAAGCCT CTAAGGCTCAAAATCACCTGTCTGCCATT
G S L G L L P I I N T A A S Y G Y Q K P L R L Q I T L S A I
1891 ACGGTGAGCACTCCAGAGGACAGCAAGCA AGCATTGGTTGAGGAGCTGCTGCTGCATT CTTGATACCGGAACGACTTTGACGTATGCT
T V S D S R G Q A S I G S A A A A L L D T G T F L Y A
1981 CCAAGCGAGATTGTCGAGAACTTGCTGAA ACCCTAGGCTTGCAGTACAGCAGCTCTGTC GGGGCTACGTGGCAAGATGCAAGGACGTT
P S E I V E K L A E T L G F D Y S S S V G A Y V A R C R D V
2071 GATAGCTACGCTGTCAACTTCGACTTCAG GGTAAAGTGATTGAAGCTCCTTGAGTTCC TTCCTGATTGCTCTGCAACCAACTCCGGA
D S Y A V N F D F Q G K V I E A P L S S F L I A L Q T N S G
2161 GAAGTTTCTCTACTGCGCATTGGGTATT TTCTCTCTGGAGACGAATCCTTCAAGCTC GCGGATCTTCTCTGCGAAACGCTACTTT
E V S S Y C A L G I F S S G D E S F T L G D T F L R N A Y F
2251 GTGGTGACCTCGAGGGATATCAAAATCGCT ATAGCTAACGTGAACCTGAATCCTGGAGCC GAGCAAATTGAGGTCTCTCAGGCAACTCC
V A D L E G Y Q I A I A N V N L N P G A E Q I E V I S G N S
2341 ATTCTTCTGCTTCTGTCGTTTCCGATTAC TCCAATACCTGGGGCGCTCTGCCACCGCT TTGGACACTGACAGGCTACTACTCTGGGA
I P S A S S V S D Y S N T W G A S A T A L D T D R P T T L G
2431 TCTGTGACTGCTGTGGCGATGAAAGAGTG ACCTCGACCAAGAAGGTTTCGAGTGTGAAG ACAAGCACTTCGTCGGGTCCGGGTCCACT
S V T A V G D E R V T S T K K V S S V K T S T S S G S Y T
2521 TCGGAGTCGTCTACGTCCAGTTCGATTCC AGCAATGGCCCAAGGACAGTAGGCTTTAGT TTGTGTGCCGTTTGTGCGCATTCTTGATT
S E S S T S S S H S ② S N G P R T V G F S I C A V I C A F I I
2611 TCTATACTAGTTGTTGCTagatctgaagt tctaaggggtttagcttcatattatgatt ttttttatttggaccgctcgaattgttt
S I I V V C
2701 ttccgacgggtctacttttaagctgcaaga tctcgitttagcgtcgitttatttctcgttcg ttttagtgacaaaaaacagaaaaaaact
2791 ataaaaagcgggtatataacctttatatttt gataaacatgagcagcgaaatgaagctagc accaaaggatttacpagaaggacaagggtt
2881 cgccaaggctctgcatggcaaggacgcccgc gagcgctacaggaatgagtgcttgggtgaa gaaggacaaggaagctcaaaaagtcgcgat
2971 ggaaggatatttcaagcactgggacgggaa aaccgacgagggagactgaaaagtcgagact cgaggactactcgagctcaccgaagcacta
3061 ctacaacctggtagcggatttctacpagta tggatggggatcctggttccacttttccag atactacaagggagagccatttagacaagc
3151 t

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FIG. 2

HpYPS1 : MKVATLFFLASSV----CVLG-----DPQFVKLEASVLRGSTYKDSQKGAKPFMLEKRADDG : 53
ScYPS1 : MKLKTVRSAVLSSLFASQVLGKIIPAANKRDDDSNKFVKLPFFKLYGDSLENGSDKKPEVRLLKRADG : 70
ScYPS2 : MKLSVLTFVVDALLVCSSIVDAGV--TDFPSLPSNENVVVKMNFQKKYGSSFENALDDTKGRTRLMTRDD : 68
ScYPS3 : MKLQLAAVATLAVL-TSPAFAGRVLP-----DGKVVKLPFTKK-----KNGDNGLSKRSNG : 50

HpYPS1 : SVTMEQNAQSFYQVETIEIGSDKQKVGVLIDTGSSOLWVMNSNNSYCSSSTKKLKR---DGPADALQKG : 120
ScYPS1 : YEEIITNQSFYSVDLEVGTTPPONVTVLVDTGSSDLWIMGSDNPYCSSNSMGSSRRRVIDKRDDSSSGG : 140
ScYPS2 : YELVELTNQNSFYSVLELDIGTPPOKVTVLVDTGSSDLWVTGSDNPYCSTKKKDTTGSSSF--KQVNKDALA : 136
ScYPS3 : HEKFVLANEQSFYSVLELAIGTPSONLTVLLDTGSAOLWVPGKGNPYCGS----- : 99

HpYPS1 : RDLSDLYNFNSPNEDNNAGFLGGWGLTTTETATQDETQTALAAQATVDCSLYGTENPSTNSFHNNGT : 190
ScYPS1 : SLINDINPFGWLTGTGSAIGP-----TATGLGGSGTATQSVPAEATMDCQYGTFTSTGSSSTFRSNNT : 205
ScYPS2 : SVVESV--F-----TEISY-----DTTIYTSEATATFDTASTSGLIDCATYGTENTSKSSTFNSNNT : 192
ScYPS3 : -----VMDCCQYGVEDKTKSSTFRANKS : 122

HpYPS1 : T-REISYADRTFARGTWGYDDVTFNQVTVNDLSLAVADETDSSTGVFGIGLRELETTYSGG---GPQHY : 255
ScYPS1 : Y-FSISYGDGTFASGTFGTVDVLDLSDNMTGLSFAVANETNSTMGVGGIGLPELEVITYSGSTASHSGKAY : 274
ScYPS2 : E-FSIAYGDTTFASGTGHDQLSLNDNMTGLSFAVANETNSTVGVLGIGLPGLESTYSGVSLSSVQKSY : 261
ScYPS3 : SPEYAAVGDGYAEGAFGQDKLYNEEDLSGLSFAVANESNSTFGVVGIGLSTLEVITYSGKVAIMDKRSY : 192

HpYPS1 : IYDNLFFKMYDQGLINRAAYSVYLNSTESSTASILFGAVDQSKYTGSGLGLPLINTAASYGYQKPLRLQI : 325
ScYPS1 : KYDNFFPIVLKNSGAIKSNTYSLYLNDSADAMEGTILFGAVDHSKYTGTLTIPIVNTLSASGSSPIQFDV : 344
ScYPS2 : TYNNFPMVLKNSGVIKSTAYSLFANDSDSKEGTILFGAVDHCKYAGDLTIPINTLQHRGYKDPICQFV : 331
ScYPS3 : EYDNFFPLFLKESGAIDATAYSLFLNDESQSSGSILFGAVDHSKYEGOLYTTPLVNLKYSQYQHPYAFDV : 262

HpYPS1 : TISAITVSDSRGQQ--ASIGSGAAAAALDTGTTLTYPSEIVEKLAETLGFDYSSSVGAYVARCRDV--D : 391
ScYPS1 : TINGIGISDSGSSNK--TLTTTKIPALSDSGTTLTYLPQTVMIAETELGAQYSSRIGYVYLDCCPSD--D : 410
ScYPS2 : TLQGLGTSGKGKEDNLTTLTTTKIPVLLDSGTTISYMPTELVKMLADQVGATYSSAYGYIEMDCIKEMEE : 401
ScYPS3 : TLQGLGL---QTDKRNITLTTLTKLPALLDSGTTLTYPQAVALLAKSLNASYSKTLGYEYTCPSD-DN : 328

HpYPS1 : SYAVNFDFFGQKVIKAPLSSFLALQTNSEGEVSSYCALGIFS-SGDESFTLGDTFLRNAYFVADLEGYQIA : 460
ScYPS1 : SMEIVDFDGGFHHINAPLSSFLSTGT---T-----CLGIIPTSDDTGTILGDSFLTNAYVYDLENLEIS : 473
ScYPS2 : ESSIIIDFDFGGFYLSNWLSDFLVTDNRNI---CILGIAPQSDPT-IILGDNFLANTYVYDLDNMEIS : 466
ScYPS3 : KTSVAEFDGGRINAPLSDFTVQTSV--GT-----CVLAIIPQAGNATAILGDSFLRNAYVYDLDNTEIS : 392

HpYPS1 : IANVNLPNGAEQIEVISGNSIPSASSVSDYSNTWGSATALDTRPTTLGSVTAVG-----DERVTSTKK : 525
ScYPS1 : MAQARYNTTSENIEIITS-SVPSAVKAPGYNTWSTASIVTGGNIFTVNSSQTASF----- : 529
ScYPS2 : MAQANFSDDGTYIEIIES-AVPSALKAPGYSTWSTYESIVSGGNMFSTAANSSISYFASSTSHSATSSSS : 535
ScYPS3 : LAQAKYGTGKENVEVIRKS-TVPSAIRAPSYNNTWSNYASATSGGNIFT-----VRTFNGTS-TATTRS : 455

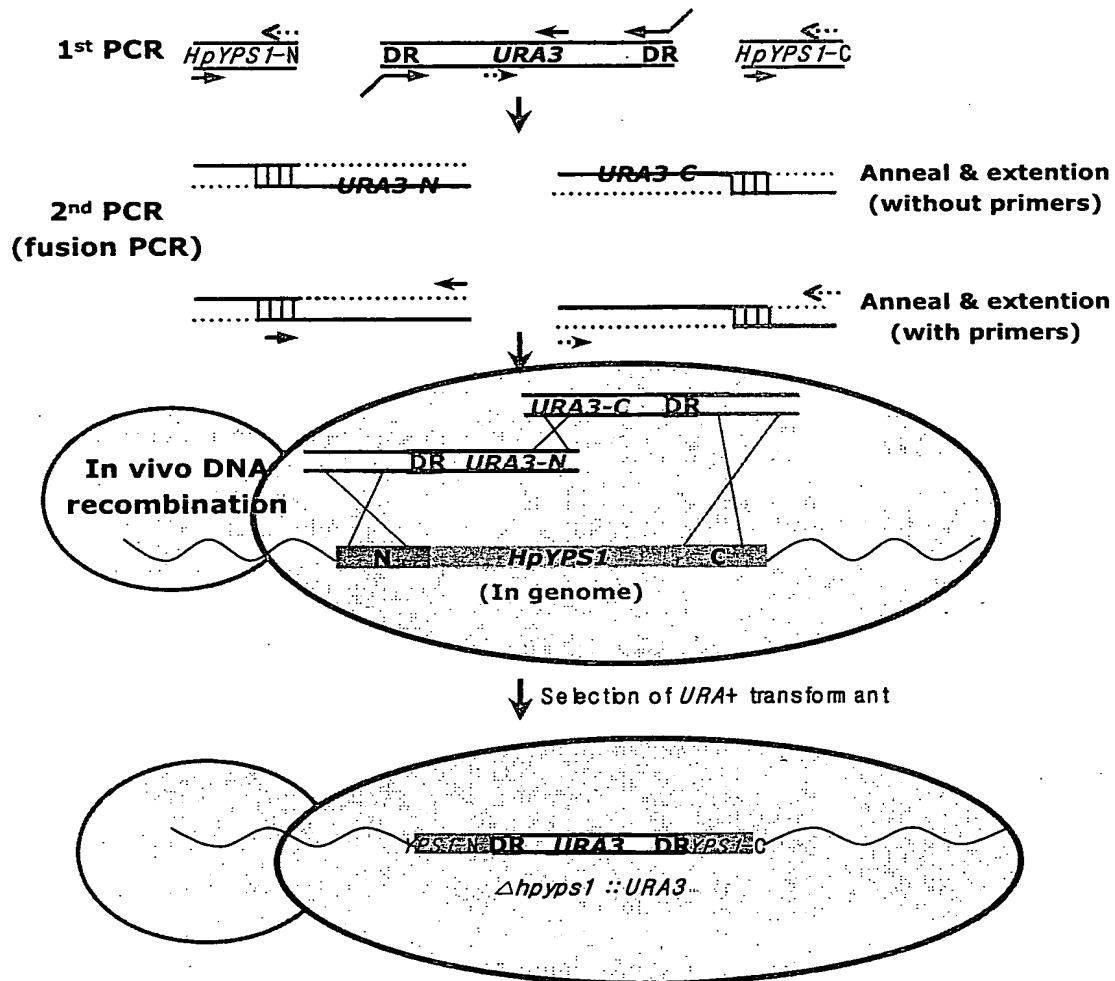
HpYPS1 : VSSVKTSTSSGSGSTSESSTSSSHS-----SNGPRTVCFSLCAVLCAFLISILV----- : 574
ScYPS1 : -----SGNLTTSTASATSTSS-----KRNVCDEHIVPSLPLTLISLLFA----- : 567
ScYPS2 : SKGQKTQTSTAALSISKSTSSSTGMLSPSTSSSPRKZNGCHNLNPPFFARFITAIFH----- : 594
ScYPS3 : TTTKKTNSTT---TAKSTHKKRALQRAATNSASSIRSTLGLLLVPSLL--LSVFFSPRHSAGSIISN : 519

HpYPS1 : -VC- : 576
ScYPS1 : --FI : 569
ScYPS2 : --HI : 596
ScYPS3 : PVYG : 523

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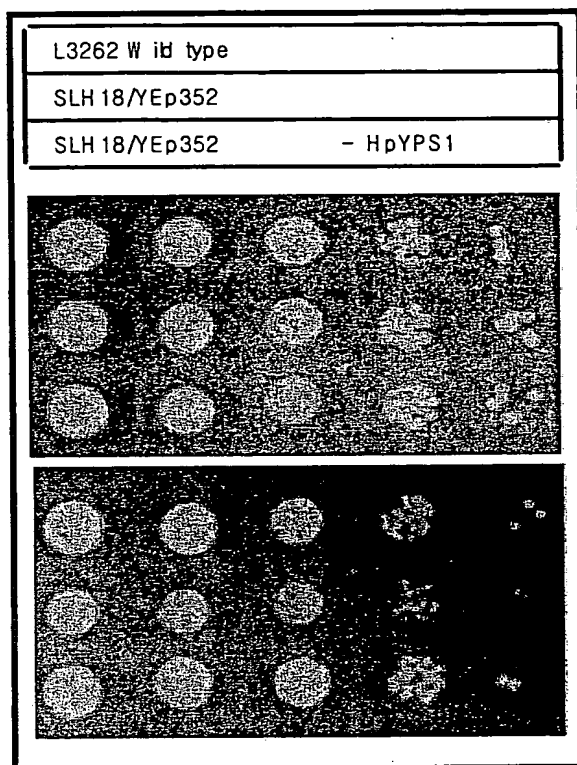
FIG. 3



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FIG. 4



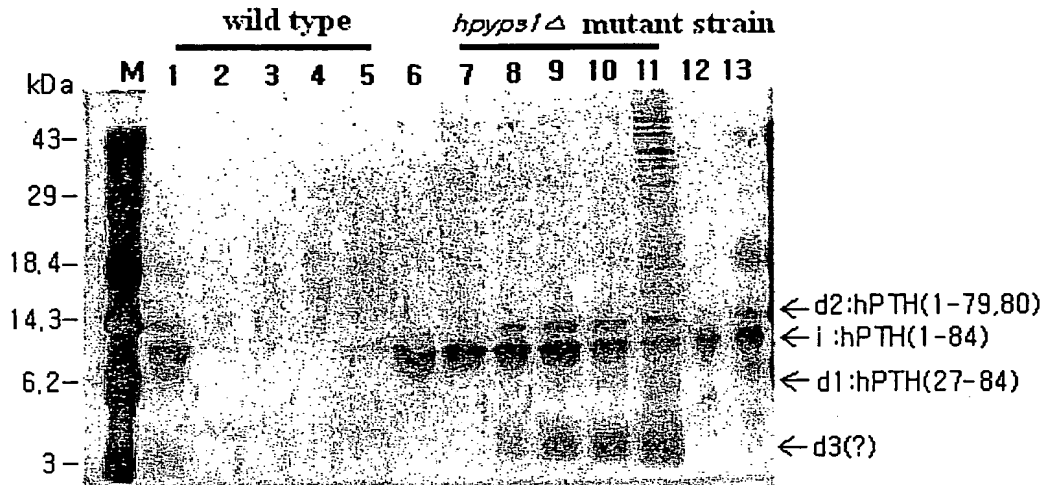
30 °C , 48 hr

37 °C , 48 hr

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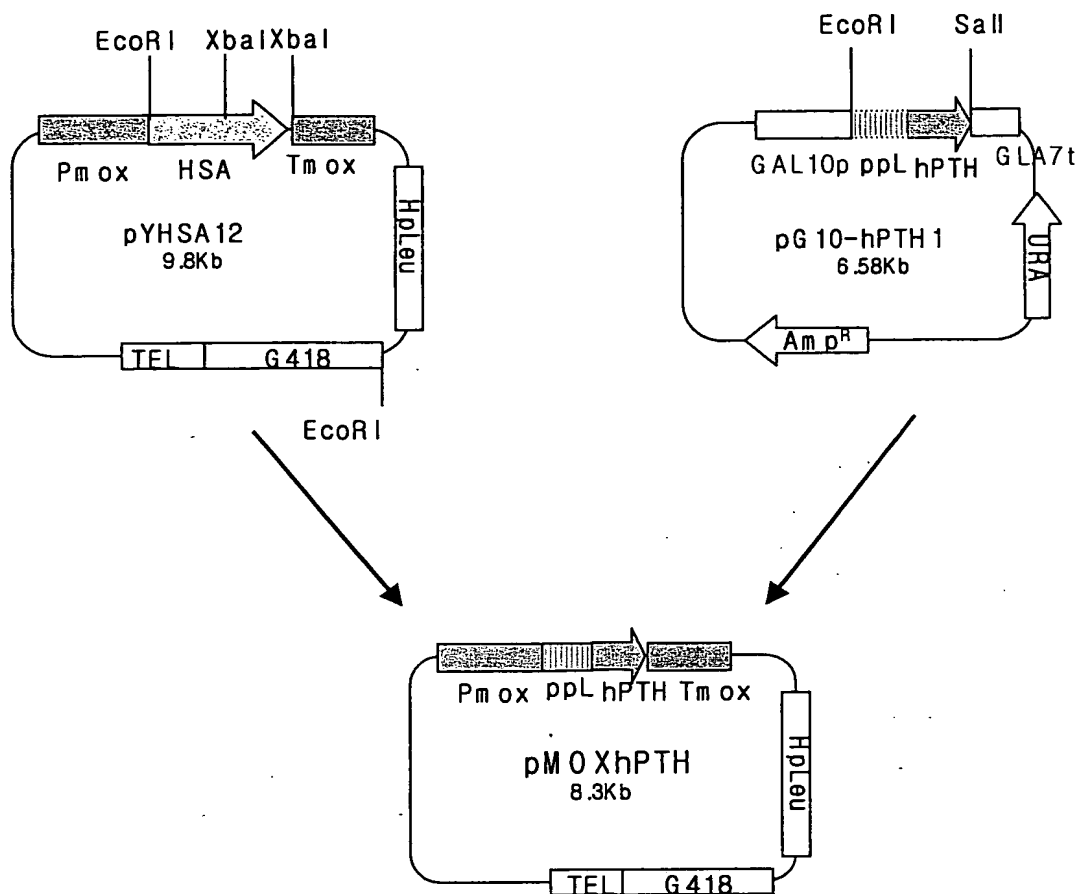
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FIG. 5

**Lane M: Molecular marker**

- 1: wild type, o-h reaction
- 2: wild type, 2-h reaction
- 3: wild type, 4-h reaction
- 4: wild type, 6-h reaction
- 5: wild type, 24-h reaction
- 6: distilled water + hPTH, o-h reaction
- 7: mutant strain, o-h reaction
- 8: mutant strain, 2-h reaction
- 9: mutant strain, 4-h reaction
- 10: mutant strain, 6-h reaction
- 11: mutant strain, 24-h reaction
- 12: hPTH 100 ng
- 13: hPTH 200 ng

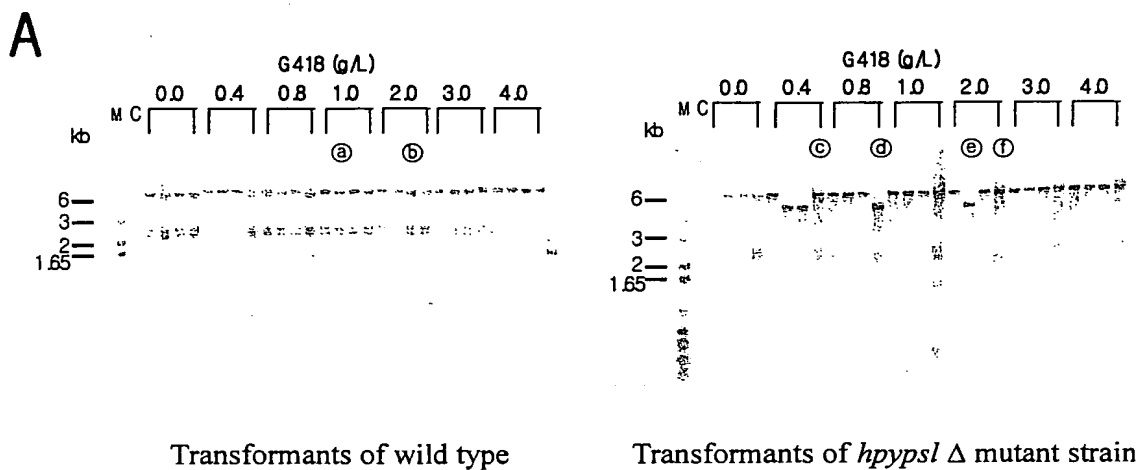
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FIG. 6

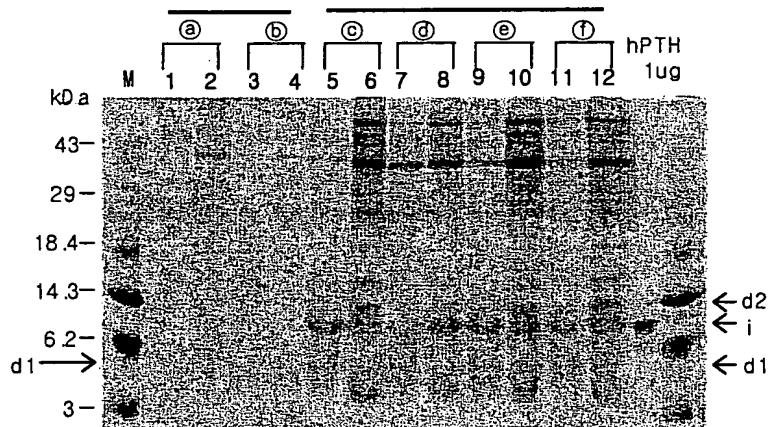
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FIG. 7

**B**

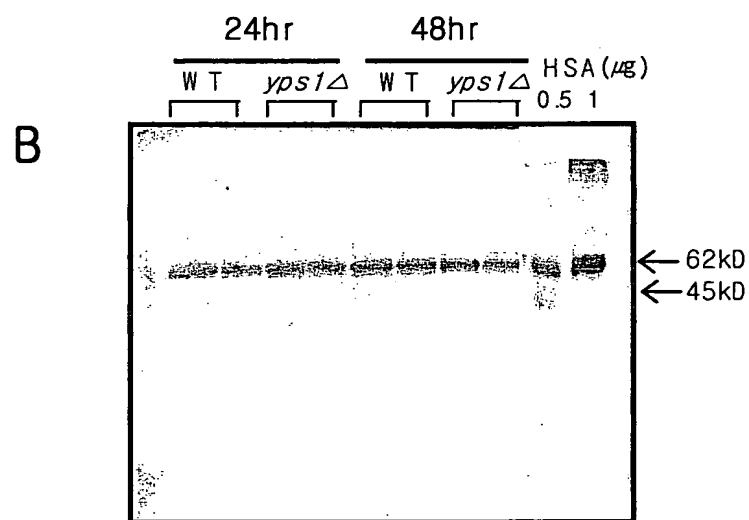
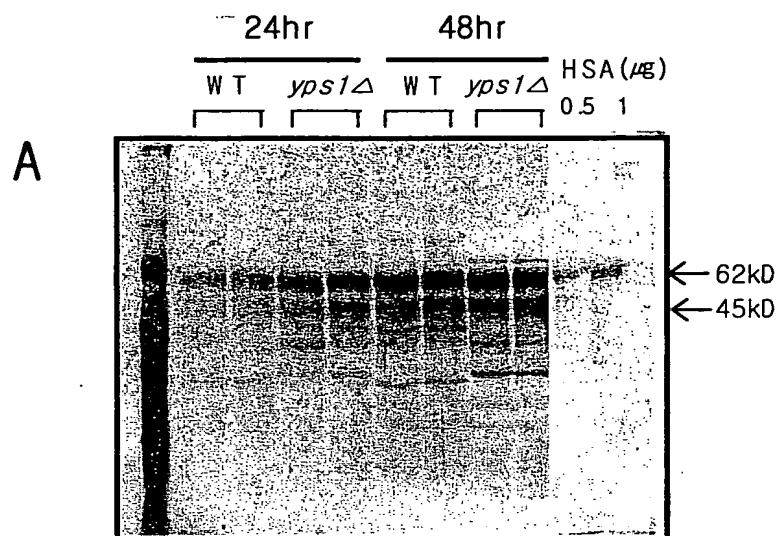
Yeast culture supernatants of wild type Yeast culture supernatants of *hpypsI* Δ mutant strain



Lane 1, 3, 5, 7, 9, 11 : 12hr after initiation of the cultivation
 Lane 2, 4, 6, 8, 10, 12 : 24hr after initiation of the cultivation

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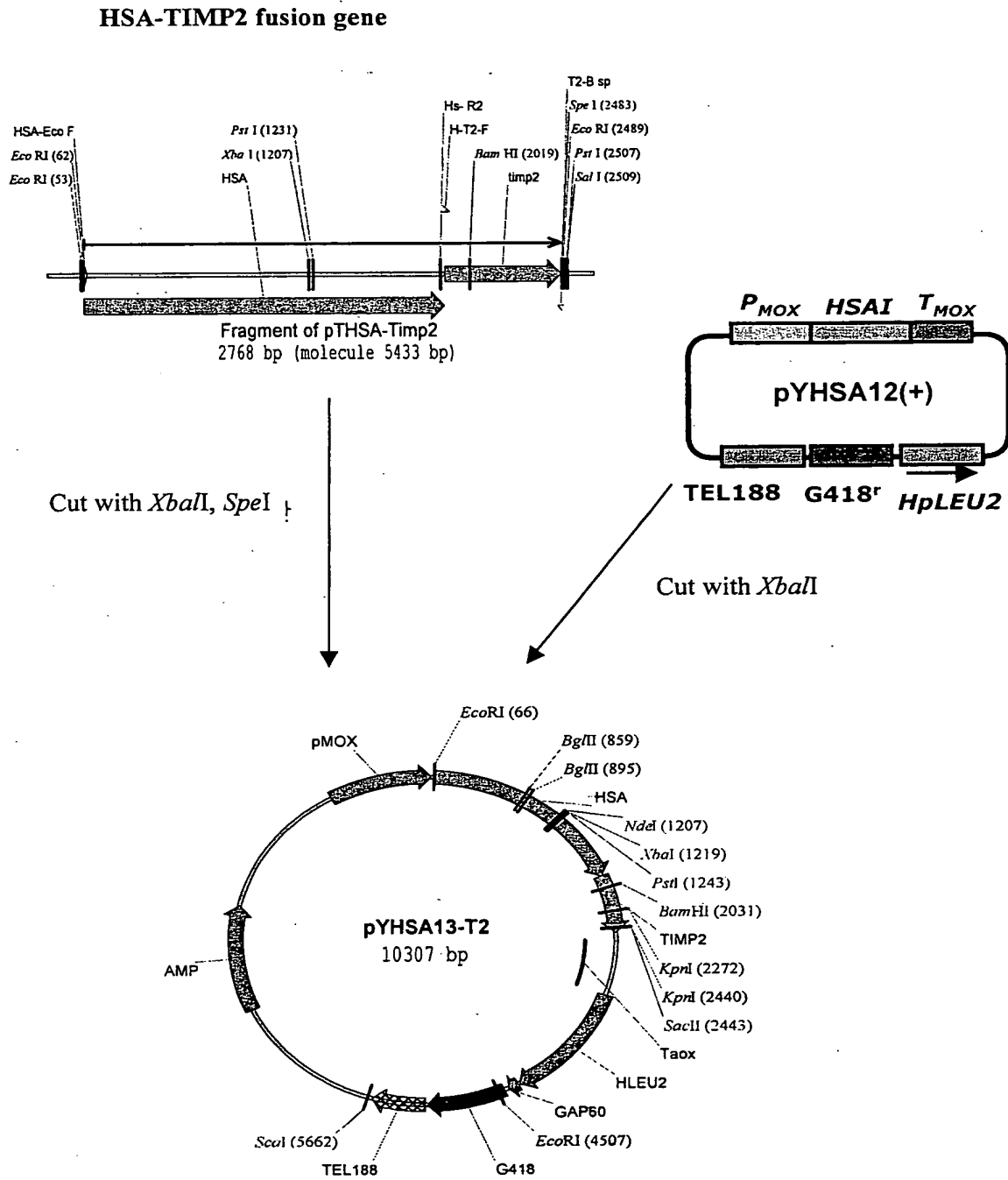
FIG. 8



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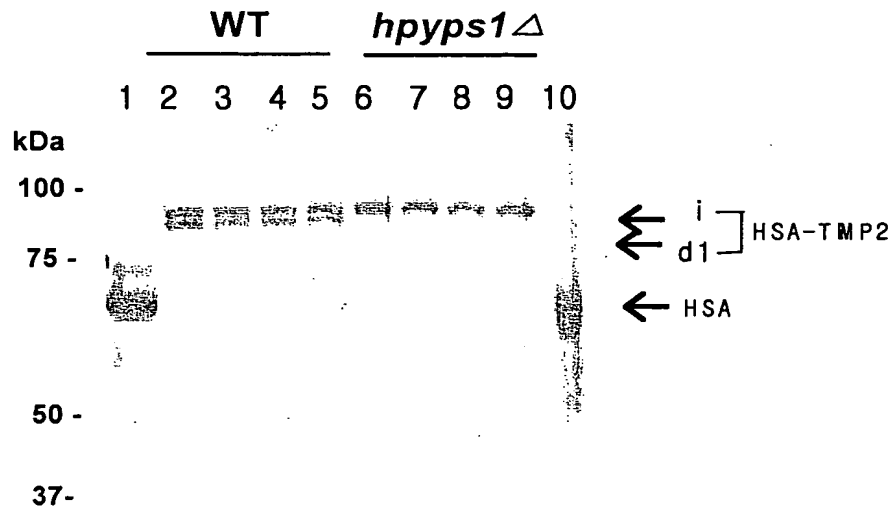
FIG. 9



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FIG. 10



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